REPORT DOCUMENTATION PAGE

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1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
10-04-2018	Final	Oct 2015 - Jan 2018

4. TITLE AND SUBTITLE

Intravenous versus intramuscular cobinamide compared to intravenous saline (control) in the treatment of acute, survivable, mitochondrial toxins in swine (Sus Scrofa): a pilot study.

5a. CONTRACT NUMBER

5b. GRANT NUMBER

FWH20150073A

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

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5d. PROJECT NUMBER

FWH20150073A

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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8. PERFORMING ORGANIZATION REPORT NUMBER

FWH20150073A

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

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10. SPONSOR/MONITOR'S ACRONYM(S)

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12. DISTRIBUTION/AVAILABILITY STATEMENT

Distribution A. Approved for public release; distribution unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Sodium azide (NaN3) poisonings are rare but extremely deadly. There is very little in the literature regarding the clinical course of sodium azide poisoning. Virtually all of the information comes from case studies and each of those describe hypokalemia hours after poisoning. Antidotes to cyanide have been used for sodium azide poisonings but have had limited success. The study was not completed, we were still in model development. What we had seen thus far is once the NaN3 infusion had begun, all pigs became hyperkalemic, acidotic and hypotensive. There were no significant differences in baseline vital signs, chemistries, or arterial blood gases including potassium (mean 4.1 mEq/L) and lactate (1.1 mmol/L) among the animals. In pigs infused with the highest dose and concentration of NaN3 (n=14), significant hyperkalemia began at apnea (5.1 mmol/L) and continued to rise (mean 7.7 mmol/L) even after the infusion was discontinued. Swine not treated for hyperkalemia died. Those treated with insulin, dextrose 50%, and calcium survived, but demonstrated elevated T waves on electrocardiogram and continued acidosis (lactate mean 6.7 mmo/L).

15. SUBJECT TERMS

hydroxocobalamin, benidipine, nitrites, sodium azide, NaN3 poisoning, toxicity, environmental, Vitamin B12a, Vitamin B12, CDC, EPA, Homeland security, swine, sus scrofa, animal testing alternatives, animal welfare, models anatomic, disease models – animals, models – biological, models – apnea, ST elevation, models

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Joseph K. Maddry
U	U	U	SAR		19b. TELEPHONE NUMBER *(Include area code)* 210-724-0654

WHASC – Animal Final Report

23Oct2017

1. Protocol Number: FWH20150073A

2. Type of Research: Animal Research

3. Title: Intravenous versus intramuscular cobinamide compared to intravenous saline (control) in the treatment of acute, survivable, mitochondrial toxins in swine (Sus Scrofa): a pilot study.

4. Principal Investigator (PI):

Name	Rank	Date of IACUC Training	Branch of Service/ Corps	Staff Resident Fellow Civilian	Department / Office Symbol	Email (if other than WHASC Outlook)	Phone	Pager
Patrick Ng	O-3	Aug 2014	Air Force	Resident	59th EMDS/SG O3D	Patrickng1@gmail.com	201-336-4407	

5. Purpose: To describe the clinical course of sodium azide poisoning and develop novel treatments for toxicity.

6. Results: The study is not complete, we are still in model development. What we have seen so far is once the NaN3 infusion began, all pigs became hyperkalemic, acidotic and hypotensive. There were no significant differences in baseline vital signs, chemistries, or arterial blood gases including potassium (mean 4.1 mEq/L) and lactate (1.1 mmol/L) among the animals. In pigs infused with the highest dose and concentration of NaN3 (n=14), significant hyperkalemia began at apnea (5.1 mmol/L) and continued to rise (mean 7.7 mmol/L) even after the infusion was discontinued. Swine not treated for hyperkalemia died. Those treated with insulin, dextrose 50%, and calcium survived, but demonstrated elevated T waves on electrocardiogram and continued acidosis (lactate mean 6.7 mmo/L).

7. How may your findings benefit the Air Force?

The CDC, EPA, and homeland security consider NaN3 to be credible terrorist threat because it is easily obtainable, highly toxic, and not detectable by smell if added to drinking water. Our findings thus far benefit the Air Force by allowing physicians to be able to adequately diagnose NaN3 toxicity.

8. Number of Animals

Projected Enrollment of Animals at the Beginning of Study: 102 (study was originally approved to study 3 toxins in 3 different arms, the toxins have since been split into their own protocols).

Actual Number of Animals Enrolled: 24

9. Status of Animals Entered into the Protocol: All animals used were in good health.

10. Number of animals since last status report:

	Number enrolled since last report	Total enrollment to date
Number of animals entered into the Study	0	24

11. Status of Funds: Our study was funded by the AF SGR. We had no budget deviations and all funds have been allocated for.

12. Reason for Closure: Our study is closing due to failure to submit annual progress report. A new protocol will soon follow.

13. Specific Problems: In conducting our study we came across a few unexpected issues including hyperkalemia and the inability to induce survivable apnea because of cardiovascular collapse. We were able to get the hyperkalemia under control and in our upcoming protocol we feel we will finally be able to induce apnea with the toxin and calcium channel blockers to treat accordingly.

14. Publications and Presentations:

Presentations:

"Sodium azide associated acute hyperkalemia in a swine model of sodium azide toxicity" Military Health System Research Symposium; Kissimmee, Florida; Aug 27-30 2017

"Sodium azide associated acute hyperkalemia in a swine model of sodium azide toxicity" SAMHS and Universities Research Forum; University of Texas at San Antonio; June 16, 2017

These Presentations and Publications have been cleared by 59 CRD and Public Affairs

Publications: None

15. Exceptional Achievements: None

16. Signature of Principal Investigator:

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SAUSREC Emergency Medicine
201-336-4407

59th Medical Wing
Institutional Animal Care and Use Committee (IACUC)
59 Clinical Research Division/SGVUS
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NOTICE OF ACTION REGARDING IACUC REVIEW

Date: 2 Jan 18

TO: Capt Patrick Ng/59 EMDS/SGO3D

Your **Final Report** was reviewed by the WHASC IACUC during the 14 Nov 17 meeting. The Committee's decision is provided below:

FWH20150073A, "Intravenous versus intramuscular cobinamide compared to intravenous saline (control) in the treatment of acute, survivable, mitochondrial toxins in swine (Sus Scrofa): a pilot study." **PI: Capt Patrick Ng/59EMDS/SGOED** The expiration date for this study is 14 Sep 2017.

Summary of main modifications to study: Amend#11 to Animal Research Protocol [Requesting to add a pre-operative Complete Blood Count and Arterial Blood Gas] [PI letter dated: 8 Aug 17] [Received: 10 Aug 17]

This amendment was not reviewed as it was noted that the study failed to meet continuing review requirements, and therefore expired and was administratively closed on 15 Sept 2017. A final report will be requested of the PI. **FOLLOW-UP: OPEN**

14 Nov 17: The PI submitted a final report and plans to submit a new protocol to complete the project.

The committee voted that this item be approved as written. **FOLLOW-UP: CLOSED**

Name of Official	**Title/Office Symbol/Phone**
MARIA E. DOMINGUEZ	Office of Research Protocol Support /SGVUS/292-6095
Signature	Info Copy To